## REMARKS

In the Office Action dated March 29, 2005, claims 1-8, 13-19, 22 and 24-31, 41 and 42, in the above-identified U.S. patent application were rejected. Reconsideration of the rejections is respectfully requested in view of the above amendments and the following remarks. Claims 1-8, 13-19, 22, 24-31, 41 and 42 are currently pending in this application, claims 20, 21, and 23 have been canceled, claims 9-12 and 32-40 have been withdrawn and claims 43 and 44 added to the application.

Claims 1-8, 13-19, 22, 24-30 and 41-42 were rejected under 35 USC §112, second paragraph, as lacking enablement. The office action indicates that the specification is only enabled for the use of cholesterol sulfate, $GM_1$, and bbG. New claims 43 and 44 are limited to the embodiments indicated as enabled by the present application. In view of this, applicants contend that this rejection should not be applied to new claims 43 and 44.

Regarding the enablement of claims 1-8, 13-19, 22, 24-30 and 41-42, applicants respectfully point out that the present invention increases the detergent solubility of protein associated with sphingolipid-cholesterol by adding gangliosides, ganglioside derivatives or cholesterol derivatives, which leads to the disruption of rafts. This finding is surprising in view of the fact that, when adding cholesterol per se, as described in the prior art, the opposite effect occurs. However, once the effect was realized, namely that disruption can be achieved by means of gangliosides, ganglioside derivatives or cholesterol

derivatives, corresponding modified derivatives could also be used to achieve the same effect. Attached are several references which show that ganglioside and cholesterol derivatives according to the present invention would produce the desired effect. In other words, the fact that the desired effect can be achieved by means of the claimed derivatives, has also been confirmed by other groups. Campbell demonstrates that replacement of a portion of cholesterol in the HIV envelope (a raft-like structure) with exogenous cholesterol analogs, i.e. epicholesterol, 4-cholestenone or coprastanol, reduced infectivity of the virus and that this activity was directly correlated with the lower raft promoting capacities of the analogs [Campbell et al., Aids(2002) 16(17):2253-61; Campbell et al., J. Virol. 2004, 78 (19):10556-65]. Page 10559 provides the structures of the cholesterol derivatives used (hydroxyl group modifications or ring structure modifications).

Using artificial model membranes, several groups have demonstrated that the styrol structure can influence the separation of phases. For instance, substances like ketocholesterol, progesterone, and pregnenolone weaken domain formation. Also derivatization of the 3-OH (cholesterol methyl ether; cholesteryl formate) had a negative effect on the microdomain stability. Moreover, sterols can determine the curvature of the microdomains inducing positive or negative curvature of the vesicles. Taken together, cholesterol derivatives have been shown to be useful for modifying sphingolipid-cholesterol domains and thus for the treatment of various diseases.

In a recent paper, Park et al., demonstrates that dietary gangliosides decrease cholesterol/ganglioside ratios, caveolin, PAF and DG content in microdomains, thus exerting a potential anti-inflammatory effect during gut development.

In view of the above discussed references and the disclosure in the present application, applicants contend that one skilled in the art would expect any and all of the derivatives recited in the present claims to be useful in the present invention and that only routine experimentation would be required to determine which other compounds are suitable for use in the present invention.

Claims 1-8, 13-19, 22, 24-30 and 41-42 were rejected under 35 USC §112, second paragraph, as indefinite. The claims have been amended to clarify that the cholesterol molecules have organic groups added or substituted on the OH function. In view of these amendments, applicants request that this rejection be withdrawn.

Applicants respectfully submit that all of claims 1-19, 22, 24-31, 41-42 and 43-44 are now in condition for allowance. If it is believed that the application is not in condition for allowance, it is respectfully requested that the undersigned attorney be contacted at the telephone number below.

In the event this paper is not considered to be timely filed, the Applicant respectfully petitions for an appropriate extension of time. Any fee for such an extension together with any additional fees that may be due with respect to this paper, may be charged to Counsel's Deposit Account No. 02-2135.

Respectfully submitted,

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